	· I	
1	ROBBINS ARROYO LLP	
2	BRIAN J. ROBBINS (190264) CRAIG W. SMITH (164886)	
3	SHANE P. SANDERS (237146) 600 B Street, Suite 1900	
4	San Diego, CA 92101	
5	Telephone: (619) 525-3990 Facsimile: (619) 525-3991	
6	E-mail: brobbins@robbinsarroyo.com csmith@robbinsarroyo.com	
7	ssanders@robbinsarroyo.com	
8	Attorneys for Plaintiff	
9	UNITED STATES	DISTRICT COURT
10	CENTRAL DISTRIC	CT OF CALIFORNIA
11	WESTERN	N DIVISION
12	RAVINDRA SINGH, Derivatively on Behalf of ARROWHEAD	) Case No.
13	PHARMACEUTICALS, INC.,	( ) ) VERIFIED STOCKHOLDER
14	Plaintiff, v.	DERIVATIVE COMPLAINT FOR BREACH OF FIDUCIARY DUTY
15	· ·	)
16	CHRISTOPHER R. ANZALONE, KENNETH A. MYSZKOWSKI, DOUGLASS GIVEN, EDWARD W.	
17	FRYKMAN, MAURO FERRARI, and MICHAEL S. PERRY,	
18	Defendants,	
19	-and-	
20	ARROWHEAD PHARMACEUTICALS, INC., a Delaware corporation,	
21		
22	Nominal Defendant.	) ) DEMAND FOR JURY TRIAL
23		,
24		
25		
26		
27		
28		

Plaintiff Ravindra Singh, by his undersigned counsel, submits this Verified Stockholder Derivative Complaint. Plaintiff alleges the following on information and belief, except as to the allegations specifically pertaining to plaintiff which are based on personal knowledge. This complaint is also based on the investigation of plaintiff's counsel, which included, among other things, a review of public filings with the U.S. Securities and Exchange Commission ("SEC") and a review of new reports, press releases, and other publicly available sources.

## **NATURE AND SUMMARY OF THE ACTION**

- 1. This is a stockholder derivative action brought by plaintiff on behalf of nominal defendant Arrowhead Pharmaceuticals, Inc. ("Arrowhead" or the "Company") against certain of its officers and directors for breaches of fiduciary duties. These wrongs resulted in hundreds of millions of dollars in damages to Arrowhead's reputation, goodwill, and standing in the business community. Moreover, these actions have exposed Arrowhead to hundreds of millions of dollars in potential liability for violations of state and federal law.
- 2. Arrowhead is a biopharmaceutical company that develops novel drugs to treat intractable diseases. ARC-520 was the Company's most important and advanced drug candidate and would have been the first Company drug to reach the U.S. market. The drug was designed to treat chronic Hepatitis B virus ("HBV") by inhibiting the production of all HBV gene products. The goal of ARC-520 was to reverse the immune suppression that prevents the body from controlling the virus and clearing the disease.
- 3. In addition to ARC-520, Arrowhead also focused on developing ARC-AAT (which treats a rare liver disease associated with a genetic disorder that causes apha-1 antitrypsin deficiency) and ARC-521 (a complimentary drug to ARC-520). These two drugs would become the Company's second and third leading candidates. All three of these drugs would be tested using EX1, a delivery

system created by the Company that transports the drugs intravenously into the patient and targets the liver.

- 4. Before Arrowhead could sell ARC-520, ARC-AAT, or ARC-521 in the United States, it has to receive approval from the U.S. Food and Drug Administration ("FDA"). In order to obtain FDA approval, the Company has to undergo a long, arduous, and expensive process that requires significant tests and trials of the drug. The first stage in the process is a Phase 1 trial which is where the company tests out a drug's safety, appropriate dosage, and side effects on a small group of people. This is followed by a Phase 2 trial which uses a larger group of patients to test a drug's effectiveness and side effects. If a drug successfully advances through these two steps, it will then be tested in a Phase 3 study and following that, the drug can be submitted to the FDA for approval.
- 5. On May 28, 2013, Arrowhead initiated the regulatory process and announced that it had filed to begin a Phase 1 clinical study on ARC-520 with the Australian Department of Health, Therapeutic Goods Administration. Subsequently, on March 3, 2014, Arrowhead announced that it had advanced the drug to a Phase 2a trial in Hong Kong where it tested sixteen chronic HBV patients.
- 6. As per FDA procedures, Arrowhead submitted its Investigational New Drug ("IND") application in December 2014, in order to test the drug in the United States. One month later, Arrowhead issued a press release stating that the FDA informed the Company that it could begin a multiple-dose Phase 2b study of ARC-520 (later titled Heparc-2004). The press release also stated that the FDA "requested a final study report from an ongoing multiple-dose non-clinical study

<sup>&</sup>lt;sup>1</sup> Sometimes a company subdivides the clinical trials such as by having a Phase 2a trial and a Phase 2b trial. Arrowhead took this approach with ARC-520.

3

4 5

6 7

10

9

12 13

14 15

16

17

18 19

20

21

23

24

25 26

27

- which has shown ARC-520 to be well tolerated with no evidence of end organ toxicity to date." This non-clinical study tested ARC-520 on primates using the EX1 delivery system.
- 7. While the Company was conducting various tests on ARC-520, ARC-AAT, and ARC-521, the Individual Defendants (as defined herein) would routinely tout the success of the Company's three leading clinical candidates. particularly focused on promoting the leading drug candidate, ARC-520, and made numerous improper statements in support of the drug. The Individual Defendants failed, however, to disclose any negative information about the drug and its adverse effects in clinical trials. Specifically, they did not disclose to the public that ARC-520 was killing primates in the Company's ongoing toxicology study which used EX1.
- 8. On November 8, 2016, Arrowhead issued a press release announcing that the FDA would be placing a clinical hold on the Company's ARC-520 clinical trial (Heparc-2004), due to deaths resulting from the primate toxicology study. This was the first time that the public was told about the serious adverse events that were associated with ARC-520 and EX1.
- 9. On this news, Arrowhead's share price fell more than 31%, or \$1.91 per share, erasing over \$133 million in market capitalization, to close at \$4.20 on November 9, 2016.
- 10. To make matters even worse for the stockholders, on November 29, 2016, Arrowhead announced that it would "discontinue development of clinical stage drug candidates" ARC-520, ARC-521, and ARC-AAT. Due to this discontinuance, the Company also announced that it would cut its workforce by approximately 30%.
- In the wake of this disclosure, Arrowhead's shares fell another 67%, or \$2.95 per share, to close at \$1.44 on November 30, 2016. By this point, the

Company's market capitalization plummeted by over \$325 million, or 76%, since the announcement that the FDA was placing a clinical hold on Heparc-2004.

12. As a direct result of this unlawful course of conduct, Arrowhead is now the subject of numerous federal securities class actions filed in the U.S. District Court for the Central District of California on behalf of investors who purchased Arrowhead's shares. Plaintiff now brings this action on behalf of the Company to rectify the harm to the Company for which the defendants are responsible.

## **JURISDICTION AND VENUE**

- 13. This Court has jurisdiction over all causes of action asserted herein pursuant to 28 U.S.C. §1332 in that plaintiff and defendants are citizens of different states and the amount in controversy exceeds \$75,000, exclusive of interest and costs. This action is not a collusive action designed to confer jurisdiction on a court of the United States that it would not otherwise have.
- 14. This Court has jurisdiction over each defendant named herein because each defendant is either a corporation that conducts business in and maintains operations in this District, or is an individual who has sufficient minimum contacts with this District so as to render the exercise of jurisdiction by the District courts permissible under traditional notions of fair play and substantial justice.
- 15. Venue is proper in this Court pursuant to 28 U.S.C. §1391 because: (i) Arrowhead maintains its principal place of business in this District; (ii) one or more of the defendants either resides in or maintains executive offices in this District; (iii) a substantial portion of the transactions and wrongs complained of herein, including the defendants' primary participation in the wrongful acts detailed herein, and aiding and abetting and conspiracy in violation of fiduciary duties owed to Arrowhead, occurred in this District; and (iv) defendants have received

substantial compensation in this District by doing business here and engaging in numerous activities that had an effect in this District.

## THE PARTIES

## **Plaintiff**

16. Plaintiff Ravindra Singh was a stockholder of Arrowhead at the time of the wrongdoing complained of, has continuously been a stockholder since that time, and is a current Arrowhead stockholder. Plaintiff is a citizen of Florida.

#### **Nominal Defendant**

17. Nominal defendant Arrowhead is a Delaware corporation with principal executive offices located at 225 S. Lake Avenue, Suite 1050, Pasadena, California. Accordingly, Arrowhead is a citizen of Delaware and California. Arrowhead develops medicines that treat intractable diseases, such as the chronic HBV, hereditary angioedema, and renal cell carcinoma. Using a broad portfolio of ribonucleic acid (RNA) chemistries and modes of delivery, Arrowhead therapies trigger the RNA interference (RNAi) mechanism to induce rapid, deep, and durable knockdown of target genes. Arrowhead operates a lab facility in Madison, Wisconsin, where the Company's research and development activities are based. As of September 30, 2016, Arrowhead had 113 full-time employees.

#### **Defendants**

18. Defendant Christopher R. Anzalone ("Anzalone") is Arrowhead's President, Chief Executive Officer, and director and has been since December 2007. Defendant Anzalone is named as a defendant in the related securities class action complaints that allege he violated sections 10(b) and 20(a) of the Securities Exchange Act of 1934. Defendant Anzalone knowingly, recklessly, or with gross negligence made improper statements in Arrowhead's press releases and public filings concerning the approval prospects, safety, and commercial viability of

ARC-520, ARC-521, and ARC-AAT. Arrowhead paid defendant Anzalone the following compensation as an executive:

Year	Salary	Stock Awards	Option Awards	Non-Equity Incentive Plan Compensation	All Other Compensation	Total
2016	\$614,051	-	\$368,797	\$448,594	\$1,889	\$1,433,331
2015	\$564,911	\$751,000	\$426,840	\$575,120	\$1,889	\$2,319,760

Defendant Anzalone is a citizen of California.

19. Defendant Kenneth A. Myszkowski ("Myszkowski") is Arrowhead's Chief Financial Officer and has been since February 2010. Defendant Myszkowski was also Arrowhead's Vice President of Finance from November 2009 to February 2010. Defendant Myszkowski is named as a defendant in the related securities class action complaints that allege he violated sections 10(b) and 20(a) of the Securities Exchange Act of 1934. Defendant Myszkowski knowingly, recklessly, or with gross negligence made improper statements in Arrowhead's press releases and public filings concerning the approval prospects, safety, and commercial viability of ARC-520, ARC-521, and ARC-AAT. Arrowhead paid defendant Myszkowski the following compensation as an executive:

Year	Salary	Stock Awards	Option Awards	Non-Equity Incentive Plan Compensation	All Other Compensation	Total
2016	\$333,178	\$307,500	\$184,383	\$130,524	\$12,431	\$968,016
2015	\$302,375	\$375,500	\$260,123	\$123,136	\$12,967	\$1,074,101

Defendant Myszkowski is a citizen of California.

20. Defendant Douglass Given ("Given") is Arrowhead's Chairman of the Board of Directors (the "Board") and has been since at least December 2012 and a director and has been since November 2010. Defendant Given knowingly or recklessly made improper statements in Arrowhead's press releases and public filings concerning the approval prospects, safety, and commercial viability of

ARC-520, ARC-521, and ARC-AAT. Arrowhead paid defendant Given the following compensation as a director:

Fiscal Year	Fees Earned or Paid in Cash	Stock Awards	Total
2016	\$75,000	\$212,250	\$287,250
2015	\$103,750	\$262,850	\$366,600

Defendant Given is a citizen of California.

21. Defendant Edward W. Frykman ("Frykman") is an Arrowhead director and has been since January 2004. Defendant Frykman was also Chairman of Arrowhead's Audit Committee and a member of that committee from at least December 2013 to at least January 2017. Defendant Frykman knowingly or recklessly made improper statements in Arrowhead's press releases and public filings concerning the approval prospects, safety, and commercial viability of ARC-520, ARC-521, and ARC-AAT. Arrowhead paid defendant Frykman the following compensation as a director:

Fiscal Year	Fees Earned or Paid in Cash	Stock Awards	Total
2016	\$50,000	\$153,750	\$203,750
2015	\$48,750	\$187,750	\$236,500

Defendant Frykman is a citizen of California.

22. Defendant Mauro Ferrari ("Ferrari") is an Arrowhead director and has been since August 2010. Defendant Ferrari was also a member of Arrowhead's Audit Committee from at least January 2016 to at least January 2017. Defendant Ferrari knowingly or recklessly made improper statements in Arrowhead's press releases and public filings concerning the approval prospects, safety, and commercial viability of ARC-520, ARC-521, and ARC-AAT. Arrowhead paid defendant Ferrari the following compensation as a director:

Fiscal Year	Fees Earned or Paid in Cash	Stock Awards	Total
2016	\$37,500	\$49,995	\$87,495

- 7 -

Defendant Ferrari is a citizen of Texas.

23. Defendant Michael S. Perry ("Perry") is an Arrowhead director and has been since December 2011. Defendant Perry was also Arrowhead's Lead Director from at least January 2016 to at least January 2017. Defendant Perry was a member of Arrowhead's Audit Committee from at least December 2013 to at least January 2017. Defendant Perry knowingly or recklessly made improper statements in Arrowhead's press releases and public filings concerning the approval prospects, safety, and commercial viability of ARC-520, ARC-521, and ARC-AAT. Arrowhead paid defendant Perry the following compensation as a director:

Fiscal Year	Fees Earned or Paid in Cash	Stock Awards	Total
2016	\$65,000	\$184,500	\$249,500
2015	\$60,000	\$225,300	\$285,300

Defendant Perry is a citizen of Colorado or Basel, Switzerland.

24. The defendants identified in ¶¶18-19 are referred to herein as the "Officer Defendants." The defendants identified in ¶¶18, 20-23 are referred to herein as the "Director Defendants." The defendants identified in ¶¶21-23 are referred to herein as the "Audit Committee Defendants." Collectively, the defendants identified in ¶¶18-23 are referred to herein as the "Individual Defendants."

# **DUTIES OF THE INDIVIDUAL DEFENDANTS**

# **Fiduciary Duties**

25. By reason of their positions as officers and directors of the Arrowhead, each of the Individual Defendants owed and owe Arrowhead and its stockholders fiduciary obligations of trust, loyalty, good faith, and due care, and were and are required to use their utmost ability to control and manage Arrowhead in a fair, just, honest, and equitable manner. The Individual Defendants were and

are required to act in furtherance of the best interests of Arrowhead and not in furtherance of their personal interest or benefit.

- 26. To discharge their duties, the officers and directors of Arrowhead were required to exercise reasonable and prudent supervision over the management, policies, practices, and controls of the financial affairs of the Arrowhead. By virtue of such duties, the officers and directors of Arrowhead were required to, among other things:
- (a) accurately guide the Company's stockholders and the public when speaking about Arrowhead's business prospects, including the commercial viability and safety of its developmental drugs;
- (b) conduct the affairs of the Arrowhead in an efficient, business-like manner in compliance with all applicable laws, rules, and regulations so as to make it possible to provide the highest quality performance of its business, to avoid wasting Arrowhead's assets, and to maximize the value of the Arrowhead's stock; and
- (c) remain informed as to how Arrowhead conducted its operations, and, upon receipt of notice or information of imprudent or unsound conditions or practices, make reasonable inquiry in connection therewith, and take steps to correct such conditions or practices and make such disclosures as necessary to comply with applicable laws.

#### **Breaches of Duties**

27. The conduct of the Individual Defendants complained of herein involves a knowing and culpable violation of their obligations as officers and directors of Arrowhead, the absence of good faith on their part, and a reckless disregard for their duties to the Company that the Individual Defendants were aware or reckless in not being aware posed a risk of serious injury to the Company.

29. The Individual Defendants, because of their positions of control and authority as officers and/or directors of Arrowhead, were able to and did, directly or indirectly, exercise control over the wrongful acts complained of herein. The Individual Defendants also failed to prevent the other Individual Defendants from taking such illegal actions. As a result, and in addition to the damage the Arrowhead has already incurred, Arrowhead has expended, and will continue to expend, significant sums of money.

#### **Additional Duties of the Audit Committee Defendants**

30. In addition to these duties, the Audit Committee Defendants, defendants Ferrari, Frykman, and Perry, owed specific duties to Arrowhead to assist the Board in "oversee[ing] the Company's auditing, accounting and control functions." Additionally the Audit Committee is tasked with "[r]eview[ing] the annual audited financial statements and Form 10K and the unaudited quarterly financial statements and Form 10-Q to be filed with the SEC."

# **CONSPIRACY, AIDING AND ABETTING, AND CONCERTED ACTION**

- 31. In committing the wrongful acts alleged herein, the Individual Defendants have pursued, or joined in the pursuit of, a common course of conduct, and have acted in concert with and conspired with one another in furtherance of their common plan or design. In addition to the wrongful conduct herein alleged as giving rise to primary liability, the Individual Defendants further aided and abetted and/or assisted each other in breaching their respective duties.
- 32. During all times relevant hereto, the Individual Defendants, collectively and individually, initiated a course of conduct that was designed to and

- 33. The Individual Defendants engaged in a conspiracy, common enterprise, and/or common course of conduct. During this time, the Individual Defendants caused Arrowhead to issue improper statements about ARC-520, ARC-521, and ARC-AAT.
- 34. The purpose and effect of the Individual Defendants' conspiracy, common enterprise, and/or common course of conduct was, among other things, to disguise the Individual Defendants' violations of law and breaches of fiduciary duty; and to conceal adverse information concerning the Company's operations, financial condition, and future business prospects.
- 35. The Individual Defendants accomplished their conspiracy, common enterprise, and/or common course of conduct by causing the Company to purposefully or recklessly release improper statements. Because the actions described herein occurred under the authority of the Board, each of the Individual Defendants was a direct, necessary, and substantial participant in the conspiracy, common enterprise, and/or common course of conduct complained of herein.
- 36. Each of the Individual Defendants aided and abetted and rendered substantial assistance in the wrongs complained of herein. In taking such actions to substantially assist the commission of the wrongdoing complained of herein, each Individual Defendant acted with knowledge of the primary wrongdoing,

substantially assisted in the accomplishment of that wrongdoing, and was aware of his overall contribution to and furtherance of the wrongdoing.

## FACTUAL BACKGROUND

- 37. Arrowhead is a biopharmaceutical company that develops novel drugs to treat intractable diseases. None of the drugs that Arrowhead has produced have ever received FDA approval to be sold in the United States. According to Arrowhead's Annual Report on Form 10-K for the fiscal year ended September 30, 2016, filed with the SEC on December 14, 2016, the Company had a net loss of \$81.7 million on revenue of approximately \$160,000 for 2016. Given the Company's weak financials, Arrowhead is dependent on raising money from the market, either through stock sales or debt issuances, in order to continue to fund its operations. The Company's stock price, therefore, is of critical importance to how much and on what terms Arrowhead can raise money. Both its stock price and other ways to raise money are dependent on purchasers and lenders' ability to trust that the Company and its fiduciaries are truthful when discussing Arrowhead's drug programs.
- 38. Arrowhead began developing its lead drug, ARC-520, in 2013 with the hope that it would become the Company's first drug to gain FDA approval and reach the market. The drug was designed to treat chronic HBV by inhibiting the production of all HBV gene products. The Company created a delivery system, EX1, in order to transmit this drug intravenously into patients. Given that ARC-520 was slated to be the Company's first drug that could be commercially sold, the drug was vital to Arrowhead's eventual profitability and growth. As such, the Individual Defendants and the market in general, have paid particularly close attention to the drug and its clinical developments.
- 39. In order for the FDA to approve ARC-520 for sale in the United States, Arrowhead had to conduct clinical trials to prove that the drug is safe and

27

2

3

4

5

6

7

8

9

10

12

13

14

15

16

17

18

19

20

21

23

24

25

- effective. On May 28, 2013, Arrowhead initiated the regulatory process and announced that it filed to begin a Phase 1 clinical study on ARC-520 with the Australian Department of Health, Therapeutic Goods Administration. On March 3, 2014, Arrowhead announced that it advanced the drug to a Phase 2a trial in Hong Kong where it tested sixteen chronic HBV patients.
- 40. As per FDA procedures, Arrowhead submitted its IND application in December 2014, in order to get the drug approved in the U.S. One month later, Arrowhead issued a press release stating that the FDA informed the Company that it could begin a multiple-dose Phase 2b study of ARC-520 (later titled Heparc-2004). The press release also stated that the FDA "requested a final study report from an ongoing multiple-dose non-clinical study which has shown ARC-520 to be well tolerated with no evidence of end organ toxicity to date." This non-clinical study tested ARC-520 on primates using the EX1 delivery system.
- 41. In June 2014, Arrowhead announced in a press release that it would begin development of ARC-AAT, a drug treatment for a rare liver disease associated with a genetic disorder that causes apha-1 antitrypsin deficiency. In September 2015, the Company announced in a press release that it was beginning development of ARC-521, a complimentary drug to ARC-520. These two drugs would become the Company's second and third leading candidates and would also be tested using the EX1 delivery system.

# **IMPROPER STATEMENTS**

42. Defendants improper statements began on January 12, 2015, when the Company issued a press release on their website titled: "Arrowhead Provides Update on IND for ARC-520 Phase 2b Study." Here, the Company announced that it was cleared by the FDA to begin the Phase 2b trial, Heparc-2004. The press release also stated that the FDA "requested a final study report from an ongoing multiple-dose non-clinical study which has shown ARC-520 to be well tolerated

with no evidence of end organ toxicity to date." Defendant Anzalone claimed "[w]e will work closely with the FDA throughout this process."

43. On May 11, 2015, Arrowhead filed its Quarterly Report on Form 10-Q for the fiscal second quarter ended March 31, 2015, with the SEC. This report highlighted positive data about ARC-520 and the clinical trials in which the drug was tested. Specifically, in the section entitled, "Management's Discussion and Analysis of Financial Condition and Results of Operation," the Form 10-Q claimed that there was "no dose-limiting toxicities or serious adverse events" observed in the Phase 2a studies of ARC-520. However the Form 10-Q made no mention of the ARC-520 primate study or the EX1 delivery system which led to multiple serious adverse events. The Form 10-Q stated:

Arrowhead Research develops novel drugs to treat intractable diseases by silencing the genes that cause them. Using the broadest portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. Arrowhead's most advanced drug candidate in clinical development is ARC-520, which is designed to treat chronic hepatitis B infection by inhibiting the production of all HBV gene products. The goal is to reverse the immune suppression that prevents the body from controlling the virus and clearing the disease. Arrowhead's second clinical candidate is ARC-AAT, a treatment for a rare liver disease associated with a genetic disorder that causes alpha-1 antitrypsin deficiency.

Arrowhead operates a lab facility in Madison, Wisconsin, where the Company's research and development activities, including the development of its RNAi therapeutics, are based. The Company's principal executive offices are located in Pasadena, California.

During the first half of fiscal year 2015, the Company continued to develop its lead clinical candidate, ARC-520, for the treatment of chronic hepatitis B as well as its second clinical candidate, ARC-AAT, an RNAi therapeutic designed to treat liver disease associated with Alpha-1 antitrypsin deficiency (AATD). *The Company continues its Phase 2a studies in ARC-520, with no dose-limiting* 

9

10

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

toxicities or serious adverse events having been observed to date. The Company submitted an Investigational New Drug application to the U.S. Food and Drug Administration in December 2014 for ARC-520 to initiate phase 2b multi-dose studies to determine the depth of hepatitis B surface antigen (HBsAg) reduction following ARC-520 injection. The Company received feedback from the FDA, and based on that feedback the Company adjusted the protocol in order to begin the trial. In April 2015, the application was approved by the FDA. The Company also expects to file with Asian and European agencies to begin additional phase 2b studies in fiscal year 2015. Additionally, the Company has initiated dosing in a phase 1 clinical trial for ARC-AAT following successful completion of the Clinical Trial Notification (CTN) regulatory process in Australia.

- 44. That same day, the Company issued a press release which again made no mention of the ARC-520 primate study or the EX1 delivery system or the multiple adverse events associated with the study and EX1. The press release highlighted the following information:
  - Started phase 1 study of ARC-AAT, the company's clinical candidate against liver disease associated with alpha-1 antitrypsin deficiency
  - Completed dosing of Part A of the ARC-AAT phase 1 study in healthy volunteers and transitioned the study into Part B which will enroll patients with PiZZ genotype alpha-1 antitrypsin deficiency

\* \* \*

- Gained clearance from the U.S. Food and Drug and Administration to begin the Heparc-2004 multi-dose Phase 2b study of ARC-520
- Filed with various regulatory authorities in Europe and Asia to explore additional multi-dose studies of ARC-520 outside of the U.S.
- Completed dosing in two additional dose cohorts in the Heparc-2001, a single-dose phase 2a study of ARC-520

Expanded Heparc-2001 to include three additional cohorts, which will be discussed on the call at 4:30 p.m. EST

3

5

9

10

11 12

13

14 15

16

17

18

19

20

21 22

23

24 25

26

27 28

45. The Individual Defendants' omissions of material information continued in subsequent public filings. On August 4, 2015, the Company filed its Quarterly Report on Form 10-Q for the fiscal third quarter ended June 30, 2015, with the SEC. This Form 10-Q reiterated largely the same positive information as the second quarter Form 10-Q (in the Management's Discussion and Analysis of Financial Condition and Results of Operation section). The Form 10-Q also contained the incorrect statement that "no serious adverse events" were observed. The Form 10-Q stated:

Arrowhead Research develops novel drugs to treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. Arrowhead's most advanced drug candidate in clinical development is ARC-520, which is designed to treat chronic hepatitis B infection by inhibiting the production of all HBV gene products. The goal is to reverse the immune suppression that prevents the body from controlling the virus and clearing the disease. Arrowhead's second clinical candidate is ARC-AAT, a treatment for a rare liver disease associated with a genetic disorder that causes alpha-1 antitrypsin deficiency.

Arrowhead operates a lab facility in Madison, Wisconsin, where the Company's research and development activities, including the development of its RNAi therapeutics, are based. The Company's principal executive offices are located in Pasadena, California.

During fiscal year 2015, the Company has continued to develop its lead clinical candidate, ARC-520, for the treatment of chronic hepatitis B as well as its second clinical candidate, ARC-AAT, an RNAi therapeutic designed to treat liver disease associated with Alpha-1 antitrypsin deficiency (AATD). The Company continues its Phase 2a studies in ARC-520, with no dose-limiting toxicities or serious adverse events having been observed to date. The Company submitted an Investigational New Drug application to the U.S. Food

and Drug Administration in December 2014 for ARC-520 to initiate phase 2b multi-dose studies to determine the depth of hepatitis B surface antigen (HBsAg) reduction following ARC-520 injection. The Company received feedback from the FDA, and based on that feedback the Company adjusted the protocol in order to begin the trial. In April 2015, the application was approved by the FDA. In June 2015, the Company received regulatory clearance in Germany for two additional Phase 2b multiple-dose studies of ARC-520 to be conducted in parallel, and also expects to file with additional Asian and European agencies to begin additional phase 2b studies.

In May 2015, the Company completed protocol-required dosing of healthy volunteers in an on-going phase 1 study of ARC-AAT, and in July 2015, initiated dosing of patients in Part B of that same study. The study recently received regulatory clearance in the United Kingdom and New Zealand. In June 2015, ARC-AAT was granted orphan drug designation by the FDA.

46. The Company also issued a press release on the same day as the Form 10-Q. In the press release, the Individual Defendants published several updates that highlighted promising developments and gave the impression to the public that the Company's two leading products were smoothly progressing through the clinical studies. The press release highlighted the following information:

# **ARC-520**

- Received regulatory permission to initiate three multiple-dose Phase 2b studies in the United States (Heparc-2004) and in Germany and Hong Kong (Heparc-2002 and 2003)
- Completed dosing of four cohorts in a single-dose Phase 2a study (Heparc-2001) and expanded the study to include three additional cohorts.
- Completed dosing in a non-clinical study in chronically infected chimpanzees that spanned more than a year
- Highlights of the Phase 2a and chimpanzee studies to be presented at an analyst day planned for September 24, 2015

ARC-AAT

- Met the dosing target for Part A of the ARC-AAT Phase 1study in healthy volunteers, and transitioned the study into Part B which is designed to enroll patients with PiZZ genotype alpha-1 antitrypsin deficiency
- Began dosing Part B of the Phase 1 study at one site in Australia
- Gained regulatory clearance to expand Part B of the Phase 1 study to allow additional sites in the United Kingdom and New Zealand
- Gained Orphan Drug Designation from the United States Food and Drug Administration
- 47. On December 14, 2015, Arrowhead filed its Annual Report on Form 10-K for the fiscal year ended September 30, 2015, signed by all of the Individual Defendants. The Form 10-K highlighted positive information about ARC-520 but once again did not include any information about the problems with the primate toxicology study or about the EX1 delivery system. Notably the Form 10-K indicated that the "ARC-520 has been well tolerated." The Form 10-K also stated that "pre-clinical results in animals" were "positive" in the ARC-520, ARC-AAT, and ARC-521 clinical trials. The Individual Defendants also discussed ARC-AAT, calling it a "promising" new drug, and announced that the Company was expanding its pipeline by adding ARC-521. The Form 10-K stated:

#### Recent Events

Arrowhead made significant progress on product and platform development during fiscal year 2015 with an expanding pipeline of RNAi therapeutics based on the Dynamic Polyconjugate (DPC<sup>TM</sup>) delivery system. The following are highlights of this progress:

\* \* \*

- 18 -

	I	
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		
12		
13		
14		
15		
16		
17		
18		
19		
20		
21		
22		
23		
24		
25		
26		
27		
28		

- Hosted an analyst day to discuss top-line findings from the Heparc-2001 Phase 2a clinical study of ARC-520 and findings from a study of 9 chimpanzees that have been treated monthly with ARC-520 for between 6 and 11 months. Key messages included the following:
  - Arrowhead's proprietary DPC<sup>TM</sup> platform can effectively and consistently knock down target genes in humans
  - o ARC-520 achieves significant HBV s-Antigen (HBsAg) reductions in humans, particularly in treatment naïve, HBeAg positive patients
  - Arrowhead identifies a large target HBV population for ARC-520 and describes a new paradigm for the HBV lifecycle
  - ARC-520 induces deep HBsAg reduction in chronically HBV infected chimps
  - o ARC-520 has been well tolerated
  - Arrowhead expands its HBV portfolio by nominating an additional clinical candidate that is complementary to ARC-520

\* \* \*

# Clinical Stage Drugs

\* \* \*

• ARC-AAT is a novel unlocked nucleobase analog (UNA)-containing RNAi-based therapeutic for the treatment of liver disease associated with Alpha-1 Antitrypsin Deficiency (AATD), a rare genetic disease that can severely damage the liver and lungs of affected individuals. The goal of treatment with ARC-AAT is to reduce the production of the mutant Z-AAT protein to prevent and potentially reverse accumulation-related liver injury and fibrosis. The Company is conducting a Phase 1b clinical trial.

48. On the same day as the Form 10-K filing, the Company issued a press release discussing findings from the Phase 2a clinical study of ARC-520 on humans and findings from a study of nine chimpanzees with chronic HBV that were treated with ARC-520 for between six and eleven months. The press release highlighted positive data from the ARC-520 trials and stated that the drug treatment was "well tolerated [with] no serious or severe adverse events were reported." Additionally the report claimed that ARC-520 led to "robust, sustained anti-viral effects" and induced "deep ... reduction" of HBV antigen levels in the chimpanzees. Notably, the Individual Defendants reported on developments concerning the human and chimpanzee trials, but still chose not to even reference the nonclinical primate study, or the problems associated with the study, or EX1, even though the study and EX1 were both vital to the drug's prospects for success. The press release stated:

## **ARC-520**

- Presented data at AASLD Liver Meeting 2014 showing statistically significant reduction in HBsAg through day 43 after a single injection (p < 0.05) in human clinical trials
- Submitted an Investigational New Drug (IND) application to the [FDA] and submitted additional clinical trial authorization applications with regulatory authorities in various jurisdictions in Europe, Asia, and Australia/New Zealand for ARC-520
- Initiated dosing in Heparc-2004, a multiple-dose Phase 2b clinical study of ARC-520 in the U.S.
- Initiated multiple-dose Heparc-2002 and Heparc-2003 Phase 2b studies of ARC-520 in Europe and Asia
- Hosted an analyst day to discuss top-line findings from the Heparc-2001 Phase 2a clinical study of ARC-520 and findings from a study of 9 chimpanzees that have been treated monthly with ARC-520 for between 6 and 11 months. Key messages included the following:

1	<ul> <li>Arrowhead's proprietary DPC<sup>TM</sup> platform can effectively and consistently knock down target genes in humans</li> </ul>
2	o ARC-520 achieved significant HBV s-Antigen (HBsAg)
3	reductions in humans, particularly in treatment naïve
4	HBeAg-positive patients
5	<ul> <li>Arrowhead identified a large target HBV population for ARC-520 and described a new paradigm for the HBV</li> </ul>
	lifecycle
7 8	o ARC-520 induced deep HBsAg reduction in chronically
	HBV infected chimpanzees
9	<ul> <li>ARC-520 was well tolerated, no serious or severe adverse events were reported in these studies</li> </ul>
11	•
	• Arrowhead expanded its HBV portfolio by nominating
12 13	ARC-521, an additional clinical candidate that is complementary to ARC-520
14	<ul> <li>Presented data at the AASLD Liver Meeting 2015 including the following:</li> </ul>
15	Tollowing.
16	<ul> <li>ARC-520 led to robust, sustained anti-viral effects in chimpanzees with chronic HBV, and we also described</li> </ul>
17	an important new discovery that HBV DNA integrated
18	into the host genome is likely an important source of HBV surface antigen (HBsAg) production
19	a In a Dhaga 2a alinical study. ABC 520 affectively
20	o In a Phase 2a clinical study, ARC-520 effectively reduced HBV viral antigens derived from cccDNA. HBV
21	surface antigen (HBsAg) was reduced substantially with
22	a maximum reduction of 1.9 logs (99%) and a mean maximum reduction of 1.5 logs (96.8%) in treatment
23	naïve e-antigen (HBeAg)-positive patients
24	<ul> <li>Presented data at Hep DART 2015 showing that ARC-520 led</li> </ul>
25	to immune reactivation in 7 of 9 chimpanzees with chronic hepatitis B infection
26	
27	ARC-AAT
28	Presented data at AASLD Liver Meeting 2014

- 6
- 7 8
- 9
- 10
- 11 12
- 13
- 14
- 1516
- 17
- 17
- 19
- 2021
- 22
- 23
- 24
- 25
- 26
- 27
- 28

- Repeat dosing of ARC-AAT in primates showed reduction of approximately 90% of serum alpha-1 antitrypsin (AAT) with long duration of effect suggesting that monthly or less frequent dosing may be sufficient for sustained suppression of hepatic AAT production
- ARC-AAT abstract highlighted in the AASLD President's Press Conference as a promising new treatment
- Filed for regulatory approval to begin a Phase 1 clinical trial of ARC-AAT for the treatment of liver disease associated with alpha-1 antitrypsin deficiency
- Initiated dosing in a Phase 1 clinical trial of ARC-AAT
- Completed dosing of Part A of the ARC-AAT phase 1 study in healthy volunteers, and transitioned the study into Part B in patients with PiZZ genotype alpha-1 antitrypsin deficiency
- Received Orphan Drug Designation from the [FDA]
- Expanded Part B of the Phase 1 study of ARC-AAT to include additional treatment sites in Europe, Australia, and New Zealand
- 49. The Individual Defendants continued their improper statements when the Company filed its Quarterly Report on Form 10-Q for the fiscal first quarter ended December 31, 2015, with the SEC on February 9, 2016. The Form 10-Q stated that "The Company continued its Phase 2 studies in ARC-520, with no dose-limiting toxicities or serious adverse events having been observed to date." The Form 10-Q focused on positive data from the ARC-520 chimpanzee study. Specifically, the Form 10-Q stated that seven out of the nine chimpanzees tested "exhibited signs of immune reactivation, which is likely a necessary step for achieving a functional cure of chronic HBV. The Company believes these data strongly support advancement of ARC-520 into Phase 2b and future clinical studies." These statements were improper because by this point the Individual

Defendants knew that ARC-520 had experienced problems in the nonclinical primate study because the Company had to inform the FDA about the primate deaths. Yet the Individual Defendants made no mention of the adverse results and instead further pushed the narrative that ARC-520 prospects were very good and that the drug was going to easily advance through clinical trials. The Form 10-Q stated:

#### **Overview**

8

5

6

7

\* \* \*

27

28

During the first quarter of fiscal year 2016, the Company continued to develop its lead clinical candidate, ARC-520, for the treatment of chronic hepatitis B as well as its second clinical candidate, ARC-AAT, an RNAi therapeutic designed to treat liver disease associated with Alpha-1 antitrypsin deficiency (AATD). The Company continued its Phase 2 studies in ARC-520, with no dose-limiting toxicities or serious adverse events having been observed to date. In connection with its Phase 2a study, the Company reported data showing that ARC-520 effectively reduced HBV viral antigens derived from cccDNA. The data showed that HBV surface antigen (HBsAg) was reduced substantially with a maximum reduction of 1.9 logs (99%) and a mean maximum reduction of 1.5 logs (96.8%) in treatment naïve e-antigen (HBeAg)-positive patients. The Company also discussed data from an ARC-520 chimpanzee study showing that in chronically HBV-infected chimpanzees treated with ARC-520 in combination with nucleoside analogs, 7 of 9 (78%) exhibited signs of immune reactivation, which is likely a necessary step for achieving a functional cure of chronic HBV. The Company believes these data strongly support advancement of ARC-520 into Phase 2b and future clinical studies. In January 2016, the Company announced that it had dosed the first patient in its Phase 2b combination study for ARC-520 and is continuing to enroll patients at multiple centers in Australia and New Zealand. The Company submitted an Investigational New Drug application to the FDA which was approved in April 2015 and the Company also received regulatory clearance in Germany for two additional Phase 2b multiple-dose studies of ARC-520 to be conducted in parallel. The Company expects to file with additional Asian and European agencies to begin additional Phase 2b studies.

1 | 2 | 3 | 4 | 5 |

Regarding ARC-AAT, the Company recently completed protocol-required dosing of healthy volunteers in an on-going Phase 1 study and initiated dosing of patients in Part B of that same study. The study recently received regulatory clearance in the United Kingdom, Germany and New Zealand, and is currently recruiting patients at several sites in those countries. In January 2016, the European Medicines Agency (EMA) granted orphan drug designation to ARC-AAT, consistent with the previous designation granted by the FDA.

50. The Company's press release issued on the same day provided additional updates showing that ARC-520 and ARC-AAT were advancing to further stages. Specifically the press release indicated that the Company "[b]egan dosing in the Phase 2b MONARCH combination study" for ARC-520 and that ARC-AAT "[r]eceived Orphan Drug Designation by the European Medicines Agency." The press release stated:

## **ARC-520**

- Presented data at the AASLD Liver Meeting 2015 including the following:
  - o ARC-520 led to robust, sustained anti-viral effects in chimpanzees with chronic HBV, and we also described an important new discovery that HBV DNA integrated into the host genome is likely an important source of HBV surface antigen (HBsAg) production
  - o In a Phase 2a clinical study, ARC-520 effectively reduced HBV viral antigens derived from cccDNA. HBsAg was reduced substantially with a maximum reduction of 1.9 logs (99%) and a mean maximum reduction of 1.5 logs (96.8%) in treatment naïve eantigen (HBeAg)-positive patients
- Presented data at Hep DART 2015 showing that ARC-520 led to immune reactivation in 7 of 9 chimpanzees with chronic hepatitis B infection
- Began dosing in the Phase 2b MONARCH combination study

#### **ARC-AAT**

1

2

3

4

5

6

7

13

14

15

16

17

18

19

20

21

22

23

24

25

26

- Expanded Part A of the Phase 1 study to test additional dose levels in healthy volunteers and expanded Part B to add additional treatment sites for patients with alpha-1 antitrypsin deficiency
- Received Orphan Drug Designation by the European Medicines Agency
- 51. On May 10, 2016, the Company filed its Quarterly Report on Form 10-Q for the fiscal second quarter ended March 31, 2016, with the SEC. The Form 10-Q repeated the same positive statements on ARC-520 as first quarter Form 10-Q. The Form 10-Q also stated the erroneous statement that "no serious adverse events" had been observed to date. Further, on the same day, the Company issued a press release that highlighted more "promising ARC-520 hepatitis B data" while again not including the adverse results from the primate study and not referencing the problems associated with EX1. The press release also provided updates on ARC-521 and ARC-AAT. The Form 10-Q stated:

#### **Overview**

Arrowhead Pharmaceuticals, Inc. develops novel drugs to treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. RNA interference (RNAi) is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing. The company's pipeline includes ARC-520 and ARC-521 for chronic hepatitis B virus, ARC-AAT for liver disease associated with alpha-1 antitrypsin deficiency, ARC-F12 for hereditary angioedema and thromboembolic disorders, ARC-LPA for cardiovascular disease, and ARC-HIF2 for renal cell carcinoma.

In April 2016, the Company changed its name from Arrowhead Research Corporation to Arrowhead Pharmaceuticals, Inc., which reflects the Company's transition to and focus on advancing products through clinical development to bring innovative new medicines to patients.

Arrowhead operates lab facilities in Madison and Middleton, Wisconsin, where the Company's research and development activities, including the development of RNAi therapeutics, are based. The Company's principal executive offices are located in Pasadena, California.

During the first half of fiscal year 2016, the Company continued to develop its lead clinical candidate, ARC-520, for the treatment of chronic hepatitis B as well as its second clinical candidate, ARC-AAT, an RNAi therapeutic designed to treat liver disease associated Alpha-1 antitrypsin deficiency (AATD). *The Company* continued its Phase 2 studies in ARC-520, with no dose-limiting toxicities or serious adverse events having been observed to date. In connection with its Phase 2a study, the Company reported data showing that ARC-520 effectively reduced HBV viral antigens derived from cccDNA. The data showed that HBV surface antigen (HBsAg) was reduced substantially with a maximum reduction of 1.9 logs (99%) and a mean maximum reduction of 1.5 logs (96.8%) in treatment naïve e-antigen (HBeAg)-positive patients. The Company also discussed data from an ARC-520 chimpanzee study showing that in chronically HBV-infected chimpanzees treated with ARC-520 in combination with nucleoside analogs, 7 of 9 (78%) exhibited signs of immune reactivation, which is likely a necessary step for achieving a functional cure of chronic HBV. The Company believes these data strongly support advancement of ARC-520 into Phase 2 and laterstage clinical studies. In January 2016, the Company announced that it had dosed the first patient in its Phase 2 combination study for ARC-520 and is continuing to enroll patients at multiple centers in Company Australia and New Zealand. The submitted Investigational New Drug application to the FDA which was approved in April 2015 and the Company also received regulatory clearance in Germany for two additional Phase 2 multiple-dose studies of ARC-520 to be conducted in parallel. The Company has also received regulatory clearance in South Korea and Hong Kong. The sites are actively recruiting and treating patients.

27

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Regarding ARC-AAT, the Company recently completed protocol-required dosing of healthy volunteers in an on-going Phase 1 study and initiated dosing of patients in Part B of that same study. The study recently received regulatory clearance in the United Kingdom, Australia, Germany, and the Netherlands, and is currently recruiting patients at several sites in those countries. In January 2016, the European Medicines Agency (EMA) granted orphan drug designation to ARC-AAT, consistent with the previous designation granted by the FDA.

In addition, the 8-K stated:

#### **ARC-520**

- Began dosing patients in three Phase 2b studies: the MONARCH study, 2007 long-term extension, and 2001 open-label extension
- Presented promising ARC-520 hepatitis B data at The International Liver Congress<sup>TM</sup> 2016, including the following key findings:
  - o ARC-520 and entecavir produced rapid HBV DNA suppression with all hepatitis B e- antigen (HBeAg) positive, treatment naïve patients achieving serum HBV DNA reductions of up to 5.5 log (99.9997%), and all HBeAg negative, treatment naïve patients achieving reductions that put them below the limit of quantitation
  - o ARC-520 effectively inhibited HBV cccDNA-derived mRNA with observed viral protein reduction in HBV patients of up to 2.0 log (99%) after a single dose
  - ARC-520 had a long duration of effect after a single dose with HBsAg still reduced by 83% after 2 months and 75% after 3 months, which is the final time point of the study
  - Based on HBsAg epitope profile analysis, poster authors and Arrowhead collaborators had previously identified a predictive hepatitis B surface-antigen (HBsAg) Clearance Profile associated with HBsAg clearance in antiviral therapy cohorts

7 8

9

10

11

12 13

14

15 16

17

24

25

26

27

28

- o There was a significant association between the development of an HBsAg Clearance Profile and ARC-520 therapy in HBV patients
- Complexed HBsAg antibodies (anti-HBs) were developed and detected in HBV patients treated with ARC-520, which may represent a recovery of the immune system response
- o After monthly administration of 6-11 doses of ARC-520 in chimpanzees chronically infected with HBV, the ARC-520 target site sequences remained virtually unchanged, indicating that no drug resistance developed during the treatment period

### **ARC-521**

• Filed for regulatory clearance to begin a Phase 1/2 first-inhuman study to assess single and multiple-doses of ARC-521 in healthy volunteers and HBV patients

## **ARC-AAT**

- Received Orphan Drug Designation by the European Medicines Agency
- 52. On August 9, 2016, Arrowhead filed its Quarterly Report on Form 10-Q for the fiscal third quarter ended June 30, 2016, with the SEC. The same day, the Company also issued a press release reiterating the "promising ARC-520 hepatitis B data" that the Company presented at the International Liver Congress The press release also indicated that the Company "[e]xpanded the 2016. MONARCH study to include additional sites, investigators, and cohorts, including patients with HBV and hepatitis Delta virus co-infection." The press release also included updates about the Company's other two leading drug candidate stating:

## **ARC-521**

Initiated a Phase 1/2 study of ARC-521 designed to evaluate the safety, tolerability, and pharmacokinetics of single doses of ARC-521 in healthy volunteers and the safety, tolerability, and

antiviral activity of single and multiple doses of ARC-521 in patients with chronic HBV. Two of a planned six normal volunteer cohorts have dosed, with the third cohort expected to dose this week

## **ARC-AAT**

- Completed enrollment in Part A of a Phase 1 study in healthy volunteers
- Received approval from regulatory authorities in Canada, Ireland, and Sweden to begin a Phase 2 study designed to determine the effect of multiple-doses of ARC-AAT on intrahepatic alpha-1 antitrypsin levels as evidenced by changes in liver biopsy in patients with alpha-1 antitrypsin deficiency

In addition, the Company's Form 10-Q stated:

#### **Overview**

Arrowhead Pharmaceuticals, Inc. develops novel drugs to treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep and durable knockdown of target genes. RNA interference (RNAi) is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing. The company's pipeline includes ARC-520 and ARC-521 for chronic hepatitis B virus, ARC-AAT for liver disease associated with alpha-1 antitrypsin deficiency, ARC-F12 for hereditary angioedema and thromboembolic disorders, ARC-LPA for cardiovascular disease, and ARC-HIF2 for renal cell carcinoma.

In April 2016, the Company changed its name from Arrowhead Research Corporation to Arrowhead Pharmaceuticals, Inc., to reflect the Company's focus on advancing products through clinical development to bring innovative new medicines to patients.

Arrowhead operates lab facilities in Madison and Middleton, Wisconsin, where the Company's research and development activities, including the development of RNAi therapeutics, are based. The Company's principal executive offices are located in Pasadena, California.

During the first nine months of fiscal year 2016, the Company continued to develop its lead clinical candidate, ARC-520, for the treatment of chronic hepatitis B as well as its second clinical candidate, ARC-AAT, an RNAi therapeutic designed to treat liver disease associated with Alpha-1 antitrypsin deficiency (AATD). The Company continued its Phase 2 studies in ARC-520, which continues to be generally well tolerated. In connection with its Phase 2a study, the Company reported data showing that ARC-520 effectively reduced HBV viral antigens derived from cccDNA. The data showed that HBV surface antigen (HBsAg) was reduced substantially with a maximum reduction of 1.9 logs (99%) and a mean maximum reduction of 1.5 logs (96.8%) in treatment naïve e-antigen (HBeAg)-positive patients. The Company also discussed data from an ARC-520 chimpanzee study showing that in chronically HBVinfected chimpanzees treated with ARC-520 in combination with nucleoside analogs, 7 of 9 (78%) exhibited signs of immune reactivation, which is likely a necessary step for achieving a functional cure of chronic HBV. The Company believes these data strongly support advancement of ARC-520 into Phase 2 and laterstage clinical studies. In January 2016, the Company announced that it had dosed the first patient in its Phase 2 combination study for ARC-520 and is continuing to enroll patients at multiple centers in Australia and New Zealand. The Company also continues to dose patients in multiple additional Phase 2 studies in Europe, Asia and the US.

53. The statements referenced in ¶¶42-52 above, were improper because the Individual Defendants allowed the omission of material information and adverse facts in press releases and public filings with the SEC. Worse, some of the published statements proved to be erroneous. The Individual Defendants knew that the statements about ARC-520, ARC-521, and ARC-AAT omitted material information, or contained incorrect information, but still allowed the improper statements to be published to the public. Specifically, they allowed the following

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

23

25

26

improper statements: (i) the Company did not observe any "serious adverse events"; (ii) the ARC-520 data was "promising"; (iii) the Company's data "strongly support[ed] advancement of ARC-520 into Phase 2 and later-stage clinical studies"; and (iv) the Phase 2 ARC-520 studies continued to be generally "well tolerated." These statements were improper because the Individual Defendants did not disclose the fact that the problems associated with the primate study and the EX1 delivery vehicle greatly jeopardized the chances that ARC-520, ARC-521, and ARC-AAT would receive FDA approval.

## THE TRUTH EMERGES

54. The truth behind the Arrowhead's business prospects and Individual Defendants' wrongdoing began to emerge on November 8, 2016. On this date, the Company issued a press release revealing that the FDA placed a clinical hold on its Heparc-2004 clinical study of ARC-520. The FDA's decision was likely due to deaths at the highest dose of an ongoing nonhuman primate toxicology study utilizing EX1. The press release stated:

Arrowhead was notified today verbally by the United States Food & Drug Administration (FDA) of its decision to place a clinical hold on Heparc-2004. The study is on hold while the company provides responses to questions arising from a nonclinical toxicology study in non-human primates using EX1, the company's liver-targeted, intravenously administered delivery vehicle.

The FDA did not indicate the clinical hold was based on any human findings. To date, EX1 has been administered over 800 times in more than 300 human study subjects and patients. Across this substantial clinical experience, only 3 serious adverse events (SAE) have been observed. Two of these were fevers, treated with acetaminophen, after which the patients continued on the study with no further complications. The other SAE was an instance of hepatic carcinoma in a patient with chronic HBV and cirrhosis, judged by the treating physician to be unrelated to the drug. A small minority (6%) of infusions in ARC-520 studies have been associated with infusion reactions, with 4 patients discontinuing ARC-520 treatment. In

addition, across the ARC-520, ARC-521, and ARC-AAT clinical programs, laboratory values have not been deemed indicative of any drug-induced organ toxicity

Arrowhead has not yet received written notice of the clinical hold from the FDA; however, based on verbal communications the clinical hold was prompted by deaths at the highest dose of an ongoing non-human primate toxicology study. This study involves higher doses of EX1 than those used clinically in humans and higher than those used in the company's previous animal toxicology studies. *The cause of these animal deaths is unknown and under investigation*. The EX1 delivery vehicle is used in the company's ARC-520, ARC-521, and ARC-AAT programs.

- 55. On this news, Arrowhead's share price fell more than 31%, or \$1.91 per share, erasing over \$133 million in market capitalization, to close at \$4.20 on November 9, 2016.
- 56. On November 14, 2016, the Individual Defendants attempted to remedy the negative press associated with ARC-520 by changing the Company's focus to ARC-AAT. Accordingly, the Individual Defendants issued a press release which focused on positive data and clinical results concerning ARC-AAT. The press release stated that "[t]he data indicate that in a first-in-human clinical study, ARC-AAT was well tolerated and induced deep and durable reduction of the target AAT protein" and "[t]he preclinical data suggest that treatment with ARC-AAT over time may improve liver health and prevent further damage."
- 57. Further, in the press release, Chief Operating Officer defendant Given stated:

We showed some exciting data today indicating that ARC-AAT, both clinically and in a preclinical model, is doing precisely what it is designed to do. In these studies, ARC-AAT led to deep, durable, and dose-dependent silencing of the liver production of the AAT protein. Accumulation of the mutant Z-AAT is believed to be the cause of progressive liver disease in patients with AATD, and reducing the production is important as it is expected to halt the progression of

liver disease. Specifically, in the clinical study ARC-AAT led to a maximum reduction of up to 90% in the highest dose group, which we believe to be near full suppression of the liver production of the protein, and a mean maximum reduction of 88%. We are also pleased that in the clinical study ARC-AAT was well tolerated at all dose levels studied (0.3 - 8 mg/kg), which is consistent with the tolerability profile of our other clinical programs that use the same  $DPC_{iv}^{TM}(EX1)$  delivery vehicle.

58. Despite the Individual Defendants' attempts to shift the attention away from the negative news on ARC-520 and the Company's flailing financials, Arrowhead's situation would become even worse. On November 29, 2016, the Company announced that it would cut its workforce by approximately 30% and "discontinue development" of ARC-520 and its complimentary drug, ARC-521. Arrowhead also announced that it would discontinue development of the Company's second leading candidate, ARC-AAT, despite the Company's announcement two weeks earlier stating that ARC-AAT "showed some exciting data" and "is doing precisely what it is designed to do." The press release stated:

The decision to discontinue development of EX1-containing programs was based primarily on two factors. First, during ongoing discussions with regulatory agencies and outside experts, it became apparent that there would be substantial delays in all clinical programs that utilize EX1, while the company further explored the cause of deaths in a non-clinical toxicology study in non-human primates. Second, Arrowhead has made substantial advances in RNA chemistry and targeting resulting in large potency gains for subQ administered and extra-hepatic RNAi-based development programs. In preclinical studies with the subQ platform, the company has obtained depth and duration of target gene knockdown approaching that of intravenously administered EX1-containing candidates, at lower doses and with good safety margins.

\* \* \*

However, due to likely regulatory considerations, as of this announcement all patient recruitment for ARC-520, ARC-521, and ARC-AAT has been halted and dosing discontinued. The company

13

11

14

15

16

17

18

19

20

21 22

23 24

25

26 27

28

will work together with investigators and clinical sites to ensure a smooth transition of study closure and patient medical care.

59. Immediately following these announcements, Arrowhead's share price fell another 67.2%, or \$2.95 per share, to close at \$1.44 on November 30, 2016. By this point, the Company's market cap plummeted by over \$325 million and decreased by 76% since the FDA announcement that it had placed a clinical hold on Heparc-2004.

# REASONS THE STATEMENTS WERE IMPROPER

- 60. The statements referenced above were each improper when made because they failed to disclose and misrepresented the following material, adverse facts, which the Individual Defendants knew, consciously disregarded, or were reckless in not knowing:
- (a) that ARC-520 and EX1 were resulting in known but publicly undisclosed health complications in various test subjects in the primate toxicology study;
- (b) the primate study was very important to ARC-520's FDA approval prospects;
- the success of ARC-520, ARC-521, and ARC-AAT was closely (c) tied to, and largely dependent on, EX1; and
- (d) as a result of the foregoing, the Individual Defendants' representations concerning the drugs were improper.

# **DAMAGES TO ARROWHEAD**

- 61. As a result of the Individual Defendants' improprieties, Arrowhead disseminated improper, public statements concerning ARC-520, ARC-521, and ARC-AAT. These improper statements have devastated Arrowhead's credibility as reflected by Arrowhead's \$325 million, or 76% market capitalization loss.
- 62. Arrowhead's statements also damaged its reputation within the business community and in the capital markets. In addition to price, Arrowhead's

current and potential customers consider a Company's ability to accurately predict and guide the public about the safety of its drugs and the drug's prospects for FDA approval. Arrowhead's ability to raise equity capital or debt on favorable terms in the future is now impaired. In addition, Arrowhead stands to incur higher marginal costs of capital and debt because the improper statements and misleading projections disseminated by the Individual Defendants have materially increased the perceived risks of investing in and lending money to Arrowhead.

- 63. Further, as a direct and proximate result of the Individual Defendants' actions, Arrowhead has expended, and will continue to expend, significant sums of money. Such expenditures include, but are not limited to:
- (a) costs incurred from defending and paying any settlement in the class actions for violations of federal securities laws;
- (b) costs incurred from continuing clinical trials on ARC-520, ARC-521, and ARC-AAT after defendants became aware that the drugs would not receive FDA approval; and
- (c) costs incurred from compensation and benefits paid to the defendants who have breached their duties to Arrowhead.

# **DERIVATIVE AND DEMAND FUTILITY ALLEGATIONS**

- 64. Plaintiff brings this action derivatively in the right and for the benefit of Arrowhead to redress injuries suffered, and to be suffered, by Arrowhead as a direct result of breaches of fiduciary duty, and violations of law, as well as the aiding and abetting thereof, by the Individual Defendants. Arrowhead is named as a nominal defendant solely in a derivative capacity. This is not a collusive action to confer jurisdiction on this Court that it would not otherwise have.
- 65. Plaintiff will adequately and fairly represent the interests of Arrowhead in enforcing and prosecuting its rights.

67. The current Board of Arrowhead consists of the following five individuals: defendants Anzalone, Given, Frykman, Ferrari, and Perry. Plaintiff has not made any demand on the present Board to institute this action because such a demand would be a futile, wasteful, and useless act, as set forth below.

# Demand Is Excused Because Defendants Face a Substantial Likelihood of Liability for Their Misconduct

- 68. As alleged above, defendants Anzalone, Given, Frykman, Ferrari, and Perry breached their fiduciary duties of loyalty by allowing and approving improper statements to be publicized, regarding the safety and approval prospects of ARC-520, ARC-521, and ARC-AAT in the Company's press releases and SEC filings. For instance, in the Company's 2015 Annual Report which was signed by all of the Board, the Individual Defendants claimed that ARC-520 was being "well tolerated" and that the "pre-clinical results in animals" were "positive" in the ARC-520, ARC-AAT, and ARC-521 clinical trials.
- 69. The Board focused the most attention to ARC-520 which was Arrowhead's most important drug and would have been the Company's first drug to reach the marketplace. Given ARC-520's significance to the Company, the Board would have closely followed all important developments regarding the drug. Specifically, the Board would have been aware of the primate toxicology results and the problems associated with EX1 because the Company had to report this data to the FDA. Accordingly, the Board would have known that FDA approval of ARC-520 was unlikely because the drug led to severe health complications and fatalities in some of the test subjects.

- ARC-AAT was also unlikely because the drugs also relied on EX1 to treat the subjects. However the Board allowed positive statements about ARC-AAT to be disseminated just fifteen days before it was discontinued. Additionally in the 2015 Annual Report, the Board stated that ARC-AAT was a "promising" drug. The Board chose to keep negative information about all three drugs private while allowing Company executives to pump out overly positive and improper information to the public. Accordingly, demand is excused because a majority of the Board faces a substantial likelihood of liability.
- 71. Defendants Ferrari, Frykman, and Perry, as members of the Audit Committee, reviewed and approved the improper statements. The Audit Committee's Charter provides that it is responsible for "oversee[ing] the Company's auditing, accounting, and control functions." The Charter also provides that the Audit Committee is tasked with "monitoring ... [t]he compliance by the Company with legal and regulatory requirements." Additionally, the Audit Committee is in charge of "[r]eview[ing] the annual audited financial statements and Form 10-K and the unaudited quarterly financial statements and Form 10-Q to be filed with the SEC." Thus, the Audit Committee Defendants were responsible for knowingly or recklessly allowing the various improper statements to be published in the Company's financial reports with the SEC. Moreover, the Audit Committee Defendants reviewed and approved the improper press releases made to the public. Despite their knowledge or reckless disregard, the Audit Committee Defendants caused these improper statements. Accordingly, the Audit Committee Defendants breached their fiduciary duty of loyalty and good faith because they participated in the wrongdoing described herein. Thus, the Audit Committee Defendants face a substantial likelihood of liability for their breach of fiduciary duties so any demand upon them is futile.

2

3

5

7

8

9

10

12

13

14

15

16

17

18

19

20

21

23

24

25

26

- 72. Plaintiff has not made any demand on the other stockholders of Arrowhead to institute this action since such demand would be a futile and useless act for at least the following reasons:
- (a) Arrowhead is a publicly held company with over 74.5 million shares outstanding and thousands of stockholders;
- (b) making demand on such a number of stockholders would be impossible for plaintiff who has no way of finding out the names, addresses, or phone numbers of stockholders; and
- (c) making demand on all stockholders would force plaintiff to incur excessive expenses, assuming all stockholders could be individually identified.

## **COUNT**

# Against the Individual Defendants for Breach of Fiduciary Duty

- 73. Plaintiff incorporates by reference and realleges each and every allegation contained above, as though fully set forth herein.
- 74. The Individual Defendants owed and owe Arrowhead fiduciary obligations. By reason of their fiduciary relationships, the Individual Defendants owed and owe Arrowhead the highest obligation of good faith, fair dealing, loyalty, and due care.
- 75. The Individual Defendants and each of them, violated and breached their fiduciary duties of candor, good faith, and loyalty.
- 76. The Individual Defendants breached their fiduciary duties to the Company by, among other things, making, issuing, approving, or failing to correct the improper statements detailed herein.
- 77. As a direct and proximate result of the Individual Defendants' breaches of their fiduciary obligations, Arrowhead has sustained significant damages, as alleged herein. As a result of the misconduct alleged herein, these

defendants are liable to the Company.

78. Plaintiff, on behalf of Arrowhead, has no adequate remedy at law.

## **PRAYER FOR RELIEF**

WHEREFORE, plaintiff, on behalf of Arrowhead, demands judgment as follows:

- A. Against all of the defendants and in favor of the Arrowhead for the amount of damages sustained by the Arrowhead as a result of the defendants' breaches of fiduciary duties;
- B. Directing Arrowhead to take all necessary actions to reform and improve its corporate governance and internal procedures to comply with applicable laws and to protect Arrowhead and its stockholders from a repeat of the damaging events described herein, including, but not limited to, putting forward for stockholder vote, resolutions for amendments to the Company's By-Laws or Articles of Incorporation and taking such other action as may be necessary to place before stockholders for a vote of the following Corporate Governance Policies:
- 1. a proposal to strengthen the Company's controls over reporting of clinical trials and developmental drugs;
- 2. a proposal to strengthen Arrowhead's oversight of its disclosure procedures;
- 3. a proposal to strengthen the Board's supervision of operations and develop and implement procedures for greater stockholder input into the policies and guidelines of the Board;
- 4. a provision to permit the stockholders of Arrowhead to nominate at least three candidates for election to the Board;
- C. Extraordinary equitable and/or injunctive relief as permitted by law, equity, and state statutory provisions sued hereunder, including attaching, imposing a constructive trust on, or otherwise restricting the proceeds

of defendants' trading activities or their other assets so as to assure that plaintiff on behalf of Arrowhead has an effective remedy; 2 Awarding to Arrowhead restitution from defendants, and each of D. 3 them, and ordering disgorgement of all profits, benefits, and other compensation obtained by the defendants; 5 Awarding to plaintiff the costs and disbursements of the action, E. 6 including reasonable attorneys' fees, accountants' and experts' fees, costs, and 7 expenses; and 8 F. Granting such other and further relief as the Court deems just and 9 proper. 10 **JURY DEMAND** 11 Plaintiff demands a trial by jury. 12 13 Dated: April 27, 2017 ROBBINS ARROYO LLP BRIAN J. ROBBINS 14 CRAIG W. SMITH SHANE P. SANDERS 15 16 /s/Brian J. Robbins BRIAN J. ROBBINS 17 600 B Street, Suite 1900 18 San Diego, CA 92101 19 Telephone: (619) 525-3990 Facsimile: (619) 525-3991 20 E-mail: brobbins@robbinsarroyo.com csmith@robbinsarroyo.com 21 ssanders@robbinsarroyo.com 22 Attorneys for Plaintiff 23 24 25 26 1160031 27 28

## **VERIFICATION**

I, Ravindra Singh, hereby declare as follows:

I am the plaintiff in the within entitled action. I have read the Verified Stockholder Derivative Complaint for Breach of Fiduciary Duty. Based upon discussions with and reliance upon my counsel, and as to those facts of which I have personal knowledge, the Complaint is true and correct to the best of my knowledge, information, and belief.

I declare under penalty of perjury that the foregoing is true and correct.

Signed and Accepted:

Dated:

**RAVINDRA SINGH**